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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/832,786	04/11/2001	David J. Diller	1073.060A	4635

23405 7590 06/25/2004

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EXAMINER

LY, CHEYNE D

ART UNIT PAPER NUMBER

1631

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

344.

Office Action Summary

Application No.

09/832,786

Applicant(s)

DILLER ET AL.

Examiner

Cheyne D Ly

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☒ Interview Summary (PTO-413)
Paper No(s)/Mail Date. 1/6/04
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 12, 2004 has been entered.

2. Claims 1-15 are examined on the merits.

CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Specific to claim 1, line 9; claim 6, lines 9 and 12; claims 3, 8, 13, line 2; and claim 11, line 11, Applicant uses the abbreviations of "rms". Abbreviations in claims are vague and indefinite unless accompanied by the full name, usually in parentheses. Claims 2, 4, 5, 7, 9, 10, 12, 14, and 15 are rejected for being dependent from claim 1, 3, 6, 8, 11, or 13.

6. Claims 1 and 6, lines 10-11; and claim 11, lines 12-13, recite the limitation "said plurality", which causes said claims to be vague and indefinite. The above claims are unclear as to whether the limitation of "said plurality" is directed to ligands, ligand-target molecule, or ligand positions. Claims 2-6, 7-10, and 12-15 are rejected for being dependent from claim 1, 6, or 11.

Art Unit: 1631

CLAIM REJECTIONS - 35 U.S.C. § 112, FIRST PARAGRAPH

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. NEW MATTER REJECTION.

9. Specific to claims 1 and 6, line 3; and claim 11, line 5, the limitation of “binding site of known geometry” has not been found in the instant specification.

CLAIM REJECTIONS - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

Art Unit: 1631

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 2, 5, 6, 7, 10-12, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ho et al. (1994) taken with Rarey et al. (1996).

13. This rejection is necessitated by Applicants amendments.

14. This rejection is maintained with respect to claims 1, 2, 5, 6, 7, 10-12, and 15, as recited in the previous office action mailed December 03, 2003.

15. Ho et al. discloses a method and a system consisting of four programs for searching for complementary components in a chemical library and the search produces 63 structures that matched at least four query requirements (page 216, column 1, lines 35-41). The method of Ho et al. is directed to the crystal structure of DHFR-NADPH from Brookhaven Protein Databank (known three-dimensional structure) (page 214, column 2, lines 24-31), as in instant claims 1, 6, and 11.

16. Foundation approximates the fit of each component with the active site. SPLICE compensates for atomic motion of the receptor atoms by decreasing the van der Waals radii to ensure each structure stably fits with the active site (known geometry). Ligands identified above are processed and clipped off until the structure is satisfactory (page 216, lines 8-48). Further, Splice screens the components in the active site and determines pairs of matched structures (page 217, lines 35-38) and images of novel ligands generated by SPLICE after matching analysis (Figure 7), as in instant claims 5, 10, and 15.

17. However, Ho et al. does not disclose the limitations of determining an rms deviation or forming clusters.

Art Unit: 1631

18. Rarey et al. discloses a method for placing molecular fragments into the active site of a receptor based on rms deviations for a receptor (Abstract etc.). The result of the method of Rarey et al. is a ranking based on minimum rms deviations (Table 5), as in instant claims 1, 2, 6, 7, 11 and 12.

19. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated to partake the concept emphasized by Ho et al. for a method and a system consisting of four programs for searching for complementary components in a chemical library and improve on it by using the method and computer of Rarey et al. to optimize the drug design process by ranking ligands based on rms deviations (page 41, lines 7-9). Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use a method and a system to search for complementary components in a chemical library as taught by Ho et al. and rank ligands based on rms deviations as taught by Rarey et al.

20. Claims 1-3, 5-8, 10-13, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ho et al. (1994) taken with Rarey et al. (1996) in view of DeLisi et al. (1996).

21. This rejection is maintained with respect to claims 1-3, 5-8, 10-13, and 15, as recited in the previous office action mailed December 03, 2003.

22. This rejection is necessitated by Applicants amendments.

23. Ho et al. discloses a method and a system to search for complementary components in a chemical library and Rarey et al. discloses a method for ranking ligands based on rms deviations as cited above, as in instant claims 1, 2, 5, 6, 7, 10-12, and 15.

Art Unit: 1631

24. However, Ho et al. and Rarey et al. do not disclose the limitations of determining an rms by using a grid.

25. DeLisi et al. discloses a method for computing the conformation and location that a protein fragment will obtain in binding to the active site by using of a grid for determining rms deviations (column 12, lines 26-64), as in claims 3, 8, and 13.

26. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated to partake the concept emphasized by Ho et al. and Rarey et al. for a method and a system to search for complementary components in a chemical library and rank ligands based on rms deviations; and improve on their methods by using a grid to determine the rms deviations as taught by DeLisi et al. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use a method and a system to search for complementary components in a chemical library as taught by Ho et al., rank ligands based on rms deviations as taught by Rarey et al. and determine the rms deviations as taught by DeLisi et al.

27. Claims 1, 2, 4, 5, 6, 7, 9-12, 14, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ho et al. (1994) taken with Rarey et al. (1996) in view of Aldenderfer et al. (1984).

28. This rejection is maintained with respect to claims 1, 2, 4, 5, 6, 7, 9-12, 14, and 15, as recited in the previous office action mailed December 03, 2003.

29. This rejection is necessitated by Applicants amendments.

Art Unit: 1631

30. Ho et al. discloses a method and a system to search for complementary components in a chemical library and Rarey et al. discloses a method for ranking ligands based on rms deviations as cited above, as in instant claims 1, 2, 5, 6, 7, 10-12, and 15.

31. However, Ho et al. and Rarey et al. do not disclose the limitations of forming clusters using a single linkage-clustering algorithm.

32. Aldenderfer et al. discloses a review of hierarchical clustering methods including single-linkage clustering algorithm (page 39-40), as in claims 4, 9, and 14.

33. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated to partake the concept emphasized by Ho et al. and Rarey et al. for a method and a system to search for complementary components in a chemical library and rank ligands based on rms deviations; and improve on their methods by using a type of hierarchical clustering algorithm such as a single-linkage clustering algorithm. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use a method and a system to search for complementary components in a chemical library as taught by Ho et al., rank ligands based rms deviations as taught by Rarey et al. and cluster using a single-linkage clustering algorithm.

RESPONSE TO ARGUMENTS

34. It is noted that Applicant does not present any arguments to accompany the instant claim amendment with the RCE, filed April 12, 2004. Applicant's arguments presented in Applicant's response, filed February 03, 2004, directed to the instant prior art rejections above have been responded to in the Advisory Action, mailed March 09, 2004. The response to Applicant's said arguments are re-iterated below.

Art Unit: 1631

35. Applicant's arguments are mainly directed to the deficiencies of the disclosure of Ho et al. and Rarey et al. in regard to the limitation of determining an rms by using a grid which has been found to be unpersuasive.

36. It is re-iterated that Ho et al. and Rarey et al. do not disclose the limitation of determining an rms by using a grid. The pointed to deficiency of Ho et al. and Rarey et al. argued by Applicant is addressed by the disclosure of DeLisi et al. It is the presence of the motivation to combine the disclosure of Ho et al., Rarey et al., and Delisi et al. as cited in the previous office action mailed December 03, 2003, which causes the claimed invention to be obvious over the prior art as a whole.

37. It is further re-iterated that DeLisi et al. discloses a method for computing the conformation and location that a protein fragment will obtain in binding to the active site by using of a grid for determining rms deviations (column 12, lines 26-64).

38. Applicant's arguments are mainly directed to the deficiencies of the disclosure of Rarey et al. in regard to the limitation of clustering of data according to the rms deviation which has been found to be unpersuasive.

39. It is re-iterated that Ho et al. and Rarey et al. do not disclose the limitation of said clustering. The pointed to deficiency of Ho et al. and Rarey et al. is addressed by the disclosure of Aldenderfer et al. It is present of the motivation to combine the disclosure of Ho et al., Rarey et al., and Aldenderfer et al. as cited in the previous office action mailed December 03, 2003, which causes the claimed invention to be obvious over the prior art as a whole.

40. Aldenderfer et al. discloses a review of hierarchical clustering methods including single-linkage clustering algorithm (page 39-40).

Art Unit: 1631

41. Applicant's argument that the Office has mischaracterized the results on Table 5 (page 49) as directed to ranking based on minimum rms deviations has been found to be unpersuasive. Applicant is directed to the footnote of Table 5 (page 49) which states solution of highest rank with an rms deviation and solution with minimal rms deviations.

CONCLUSION

42. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

43. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Art Unit: 1631

44. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

45. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

46. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

C. Dune Ly
6/20/04

Ardin H. Marschel 6/23/04
ARDIN H. MARSCHEL
PRIMARY EXAMINER